

Stability Storage: the Case for Outsourcing

By Patrick Jackson at
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While some companies will always prefer 100% control of their own storage, outsourcing stability storage requirements to an experienced contract organisation can bring significant cost-benefits – leaving companies to focus their internal resources on drug development and production.

Many leading pharmaceutical companies run their own stability storage and testing facilities in-house, and purchase their stability suites from one of the major equipment manufacturers. The range of equipment required is wide-ranging and can potentially include controlled environment rooms, biological cabinets, and pharmaceutical fridges and freezers.

Healthy competition certainly makes business an ongoing challenge for all companies as they strive for ever-increasing quality standards, allied to overall cost reduction wherever possible. We all share common issues – many of them related to finding extra resources and, when secured, using them to their fullest potential. This is where outsourcing can play a valuable part in a company's stability testing regime.

Pharmaceutical and biotechnology companies that choose to utilise the expertise of a contract stability storage organisation for the storage of their products stand to benefit initially from such a move as it eliminates the need for large capital outlay on stability chambers or rooms. A second advantage is that it reduces the requirement for costly laboratory space, and a third is that it eliminates the need to regularly service and

calibrate equipment, as this is all part of the stability storage company's remit.

Other factors that can often be overlooked when considering outsourcing include the requirement for 24/7 engineering cover and, of equal importance, disaster recovery planning in the event that a room or chamber failure cannot be rectified in the requisite time-frame.

CHOOSING THE RIGHT PARTNER

The benefits of outsourcing may be substantial but how do you choose the right partner? When looking to outsource stability storage, it is important to thoroughly appraise the company first. Factors to consider include:

- ◆ The length of time the company has been undertaking stability storage
- ◆ The availability of a team of validation engineers
- ◆ Financial stability
- ◆ Computerised monitoring systems and effective sample tracking software
- ◆ Flexibility of both the company and its staff
- ◆ The capability to accept small and large studies
- ◆ Sufficient equipment and back-up facilities
- ◆ Comprehensive alarm systems
- ◆ Service engineers on call around the clock

Only the right partner can help a company get the best from its stability storage function. Experience counts – and choosing a partner that understands specific market sectors will ensure a more efficient process and thus help drive the business forward. The service provider must offer an extremely cost-effective solution for controlled environmental storage of materials at temperatures ranging from -197°C to +60°C, and humidities ranging from 10% to 95% RH.

Figure 1: Storage at -86°C





A CONTROLLED ENVIRONMENT

It is the norm for controlled environment rooms to be built and validated to provide the climatic conditions specified in the ICH Guidelines, simulating the conditions for all four climatic zones for long-term, intermediate and accelerated testing. The company providing outsourced storage must also be able to provide unique conditions, as there are many instances where drugs and drug-related products need to be stressed/tested at conditions outside of ICH guidelines.

Temperature and humidity control is crucial. Humidity must be generated 'on demand' by high-efficiency humidifiers featuring ultrasonic transducers, as changes in temperature and/or humidity can put considerable stress on storage samples, and potentially lead to inaccurate or unsuccessful results. It is therefore essential that the temperature and humidity within each stability storage room or cabinet is strictly monitored, and that the chambers are routinely validated.

Regular validation to ensure the accurate and repeatable performance of an environmental room or cabinet is essential. At Vindon, we use a combination of UKAS (United Kingdom Accreditation Service) calibrated probes and state-of-the-art data acquisition systems to ensure that the temperature and humidity of all our rooms are monitored at all times. Typical systems are Eurotherm 6000 series data loggers which are 21 CFR Part II-compliant; this is a requirement that no data can be tampered with without leaving an audit trail. Performance-mapping tests are also undertaken annually for temperature and humidity. This ensures that the room and system are operating correctly, and that the probes have not 'drifted' from their set points. All documentation is designed to show compliance with relevant guidelines and to meet requirements.

For some pharmaceutical companies, there may be slightly different needs and special environments and protocols will need to be set up. Different conditions are certainly required for some of the emerging markets in Asia and the Middle East. Even if, strategically, the preference is to continue to run an in-house operation, it may still be worth considering a third party for handling, for example, retained samples, secondary storage, storage of quarantine samples, freeze/thaw testing and aerosol testing.



UNIFORM CONDITIONS

It is imperative that stored samples are all exposed to the same uniform, identical, repeatable and reproducible conditions. All chambers must have pre-conditioned air flow circulation to ensure uniformity for all test samples on all shelves. In addition, the stability storage chambers have to be temperature and humidity mapped, and they should operate independently with separate real-time temperature and humidity controls as and when applicable. Most of the modern rooms currently available are monitored by computer-controlled logging systems so that alarms are recorded immediately. Should a room or cabinet alarm go off, there can be an immediate response from one of the technicians available to deal with the problem straightaway. Loss of valuable samples can delay an important project and be very costly to an organisation.

The contract storage facility should be capable of accommodating all ICH and non-ICH conditions, as well as new conditions, and the contract stability storage company must be able to provide a range of requirements easily and effectively, and have sufficient room in its facility to accept more storage space when required.

STABILITY SAMPLE TRACKING

Effective stability sample tracking is extremely important; managing thousands of stability samples for different companies all with different protocols requires a solid stability sample tracking system to ensure that all samples are handled correctly. When samples are outsourced properly, identification of each sample is essential to prevent confusion when pulling stability samples from the

Figure 2:
Pharmaceuticals in
stability storage room



Figure 3: Walk-in stability storage rooms in Vindon's Stability Suite

chambers. Samples should be clearly labelled – typically with quantity, storage conditions, product name, product code, lot number and date of manufacture. Reliable stability software can also make a significant difference when tracking pull dates and sample locations and quantities; it is important to comply with regulations for audit trails and security compliance in order to meet inspection regulations.

BULK PHARMACEUTICAL CHEMICALS

Pharmaceutical products are manufactured using bulk pharmaceutical chemicals and, as such, manufacturers of inactive ingredients have to comply with GMP guidelines. Although the GMP regulations apply only to finished dosage forms, the US Federal Food, Drug, and Cosmetic Act requires that all drugs be manufactured, processed, packed, and held in accordance with current good manufacturing practice. No distinction is made between bulk pharmaceutical chemicals and finished pharmaceuticals, and the failure of either to meet cGMP standards constitutes a failure to comply with the requirements of the Act.

Stem cell storage is, however, still very much in its infancy, but there is little doubt that stem cell storage will be the norm in years to come – not just in the private sector but also in the public arena. Stem cells can easily be collected from the umbilical cord of a newborn baby and then stored under cryogenic conditions (usually at minus 190°C) in special tanks containing liquid nitrogen. At Vindon, we are currently constructing a cryobank to satisfy the needs of this emerging market.

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Figure 4: Regular validation of stability storage rooms and cabinets is essential

During the development of a pharmaceutical product and after its manufacture, the stability of the chemical constituents should be analysed according to a stability study programme that will reveal any stability issues. Undetected changes in raw materials specifications, or subtle changes in manufacturing procedures, may affect the stability of bulk pharmaceutical chemicals. Stability samples should be stored in containers that are very similar to the packaged finished product, as they would appear on the pharmacy shelf. It is also recommended by the FDA that additional samples be stored under stressful conditions (for example, elevated temperature, light, humidity or freezing) if such conditions can be reasonably anticipated. A complete range of World Climatic ICH conditions for the stability storage of bulk pharmaceutical chemicals should be available to the industry. There is also a need for complete flexibility in terms of setting up chambers to reproduce other environments to meet specific product and client requirements.



Figure 5: Putting pharmaceuticals on store in Vindon's Stability Suite

ULTRA-LOW TEMPERATURE STORAGE

There are some well-established, finely-tuned methods of preserving biological materials by freezing and storing them at ultra low or cryogenic temperatures (-86°C). The provision of a secure low temperature and ultra low temperature storage facility for samples and laboratory research materials is often required, and any such facility should ideally provide for a single box of samples – up to virtually any volume – all the way through to completion of a research project.



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For cryogenic storage, constant monitoring is normally performed with a paperless data logging system that, ideally, should also be compliant with the requirements of the US Code of Federal Regulations.

BACK-UP SECONDARY STORAGE

The probability of any company experiencing fire, power-cuts, flood, storm or any other potential disaster is distinctly uncertain, but any one of these events could significantly affect a company's stability storage and testing operations. Commercial organisations are increasingly reviewing their approach to disaster recovery plans; the objectives of any such plan can be summarised as follows:

- ◆ To minimise potential economic loss
- ◆ To insure against the loss of products in storage
- ◆ To counteract the disruption to stability storage activities
- ◆ To reduce critical loss to a company
- ◆ To provide an orderly recovery of product

One potential way forward could be to maintain an in-house stability storage suite and then, in parallel to this, a set of duplicate samples could be retained by a third party in a different but secure second geographical location. This approach is well worth considering in that it virtually eliminates the risk of a disaster scenario destroying a company's valuable stability storage samples, and causing commercial damage to the organisation.

CONCLUSION

In recent times, there has been a trend in the industry to move away from in-house stability storage towards the use of third parties. Clearly this will depend on company strategy – some organisations will always prefer 100% control of their own storage. In many cases, however, it can make sense to outsource stability storage requirements to an experienced operator based elsewhere. This kind of move needs careful thought in terms of price, quality of service and flexibility of approach; in essence, while storage would take place elsewhere, actual testing would continue to be handled in-house.

In view of the current financial crisis, the option of storing materials under controlled ICH and non-ICH conditions in a purpose-designed off-site stability suite can reap significant cost-benefits. Once the decision has been made to outsource stability storage, pharmaceutical companies can then focus their internal resources on their core competencies, and concentrate their efforts on new drug development.